PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
X-16090		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/007702	09.03.2005	15.03.2004

International Patent Classification (IPC) or national classification and IPC

C07D209/08, C07D409/12, C07D405/12, A61K31/4045, A61P3/04, A61P3/10, A61P25/24, A61P25/28, A61P25/30

Applicant

ELI LILLY AND COMPANY et al.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 10 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.12.2005	01.03.2006

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Cortés, J

Telephone No. +49 89 2399-8206

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2005/007702

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-3, 5, 7-11, 13-38	as originally filed
4, 6, 12	received on 12.12.2005 with letter of 12.12.2005

Claims, Numbers

1-23	received on 12.12.2005 with letter of 12.12.2005

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19-22

because:

☒ the said international application, or the said claims Nos. 19-22 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-23
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-23
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18, 23
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item I

Basis of the opinion

With letter of 12.12.2005 the Applicant has filed an ameded claim set amended pages 4 and 12 of the description

The main changes concern the deletion of the term "prodrug" in claims 1 and 2, the introduction of the specification for the variable n (n=1, 2 or 3) in claim 1 as well as the introduction of two different provisos in claims 1 and 2.

The variable n was defined e.g. in claim 2 as originally filed. It can therefore be assumed that the omission of this definition is claim 1 as originally filed was an obvious mistake.

The new provisos are aimed at excluding novelty relevant compounds of D3 and D4. D3 and D4 disclose compounds of a different pharmacology and medical uses and could thereofore be regarded as "accidental" anticipations.

The amendments are therefore in line with Article 34(b) PCT.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 19-22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion with regard to the industrial applicability will be formulated for these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents have been cited in the International Search Report:

D1: WO 03/101963 A (ELI LILLY) 11 December 2003 (2003-12-11)

D2: WO 02/051805 A (BAYER) 4 July 2002 (2002-07-04)

D3: YEE ET AL: "A novel series of selective leukotriene antagonists: exploration and optimization of the acidic region in 1,6-disubstituted indoles and indazoles" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 9, 1990, pages 2437-2451, XP002332451

D4: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1996, RAFALSKI, M. ET AL: "Synthesis and biological evaluation of substituted benzimidazoles - potential GPIIb/IIIa receptor antagonists" XP002332455 retrieved from STN Database accession no. 1996:696065

Novelty (Article 33(2) PCT)

Since the present claim set encompasses "prodrugs" of the structurally defined compounds of the formulae I and II, claims 1-16 and 18 are not novel in view of D3 and D4, as the compounds disclosed therein are e.g. amides of the present compounds which can be hydrolysed in vivo to compounds of the present invention.

The present compounds differ from the compounds in D1 in the benzofused heterocyclic structure and from the compounds in D2 in that the benzofused heterocycle is linked at its 1-position with the second cycle.

The compounds of D3 and D4 have been excluded from the present scope by the introduction of two different provisos in claims 1 and 2.

Inventive Step (Article 33(3) PCT)

D1 discloses opioid receptor antagonists and D2 discloses compounds for the treatment of e.g. obesity. D1 can be regarded as the closest prior art.

The problem of the present invention was the provision of new opioid receptor antagonists for the treatment of e.g. obesity.

The present compounds are structurally unrelated with the compounds of D1 and the

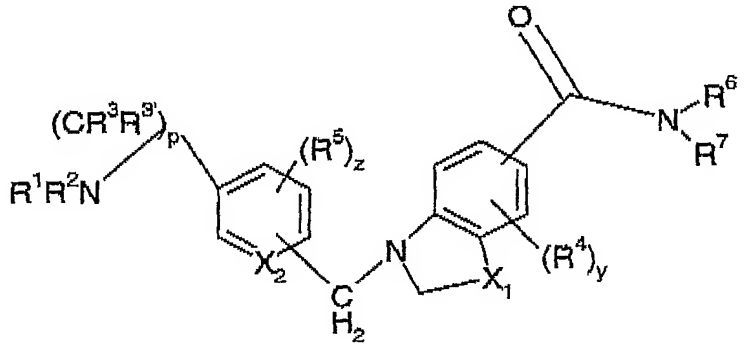
position of the linkage between the benzofused heterocycle and the second cycle is not suggested by D2 and/or D1. D3 and D4 disclose compounds with a different pharmacology and medical uses.

The present invention is therefore based on an inventive step.

Replacement 4

R^3 and $R^{3'}$ are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, aryl, C_1-C_8 alkylcycloalkyl, and C_1-C_8 alkylaryl;
R^4 and R^5 are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkoxy, halo, C_1-C_8 haloalkyl, phenyl, aryl, C_1-C_8 alkylaryl, $(CH_2)_mNSO_2C_1$-C_8 alkyl, $(CH_2)_mNSO_2$phenyl, $(CH_2)_mNSO_2$aryl, $-C(O)C_1$-C_8 alkyl, and $-C(O)OC_1$-C_8 alkyl; wherein each R^4 and R^5 is attached to its respective ring only at carbon atoms; wherein m is 1 or 2; and n is 1, 2, or 3;
R^6 and R^7 are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, $C(O)C_1$-C_8 alkyl, SO_2C_1-C_8 alkyl, SO_2C_1-C_8 alkylaryl, SO_2C_1-C_8 alkylheterocyclic, aryl, C_1-C_8 alkylaryl, C_3-C_7 cycloalkyl, C_1-C_6 alkylcycloalkyl, $(CH_2)_mC(O)OR^8$, $(CH_2)_mC(O)R^8$, $(CH_2)_mC(O)NR^8R^8$, and $(CH_2)_mNSO_2R^8$; wherein each of the alkyl, alkenyl, and aryl groups are optionally substituted with one to two groups independently selected from C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, and C_1-C_8 alkylaryl; and wherein R^6 and R^7 may independently combine with each other, and with the nitrogen atom to which they are attached to form a 4, 5, 6, or 7-membered nitrogen containing heterocycle which nitrogen containing heterocycle may optionally have substituents selected from the group consisting of oxo, amino, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, and C_1-C_8 alkylaryl;
R^8 is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, benzyl, and C_5-C_8 alkylaryl; or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer, or mixture of diastereomers thereof.

The present invention also provides a compound of formula II



II

wherein p is 0, 1, or 2;

Replacement 6

R^8 is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, benzyl, and C_5-C_8 alkylaryl; or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer, or mixture of diastereomers thereof.

The present invention also provides a method for the prevention, treatment and/or amelioration of the symptoms of obesity and Related Diseases comprising administering a therapeutically effective amount of a compound of formula (I) or II or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer or mixture of diastereomers thereof.

The present invention also provides a pharmaceutical formulation comprising a compound of formula I or II in association with a carrier, diluent and/or excipient.

The present invention also relates to a method for the treatment and/or prophylaxis of obesity and Related Diseases including eating disorders (bulimia, anorexia nervosa, etc.), diabetes, diabetic complications, diabetic retinopathy, sexual/reproductive disorders, depression, anxiety, epileptic seizure, hypertension, cerebral hemorrhage, congestive heart failure, sleeping disorders, atherosclerosis, rheumatoid arthritis, stroke, hyperlipidemia, hypertriglycemia, hyperglycemia, hyperlipoproteinemia, substance abuse, drug overdose, compulsive behavior disorders (such as paw licking in dog), and addictive behaviors such as for example, gambling, and alcoholism, comprising administering a therapeutically effective amount of a compound of formula I or II or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer or mixture of diastereomers thereof.

The present invention relates to a compound of formula I or II useful for the manufacture of a medicament for the treatment, prevention and/or amelioration of symptoms associated with obesity and Related Diseases.

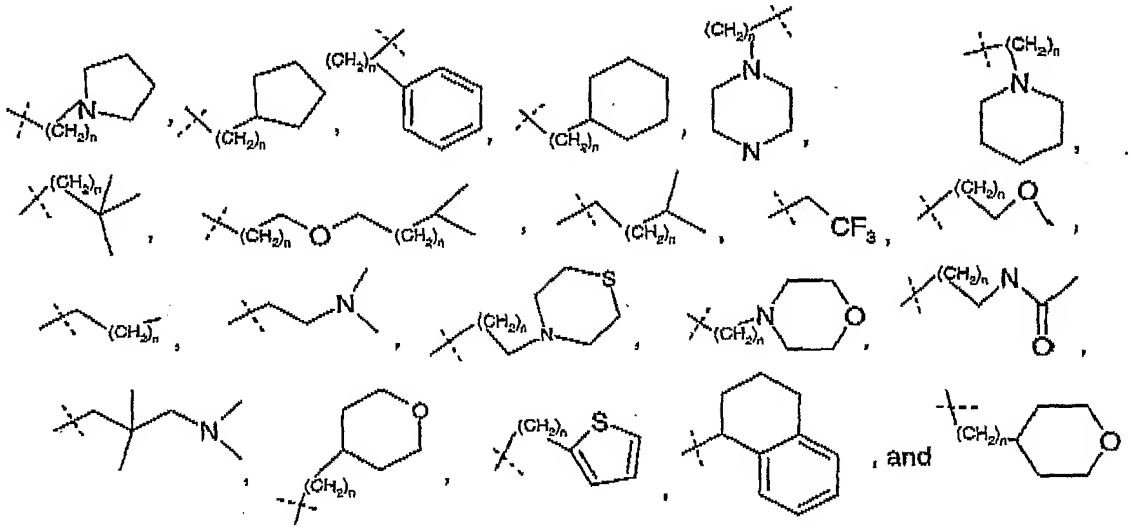
In another embodiment, the present invention relates to a compound of formula I or II or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer or mixture thereof, useful as an appetite suppressant.

The present invention relates to a method of achieving weight loss while maintaining lean muscle mass or minimizing the loss of lean muscle mass comprising administering a compound of formula I or II or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer or mixture thereof, to a patient in need thereof.

Replacement 12

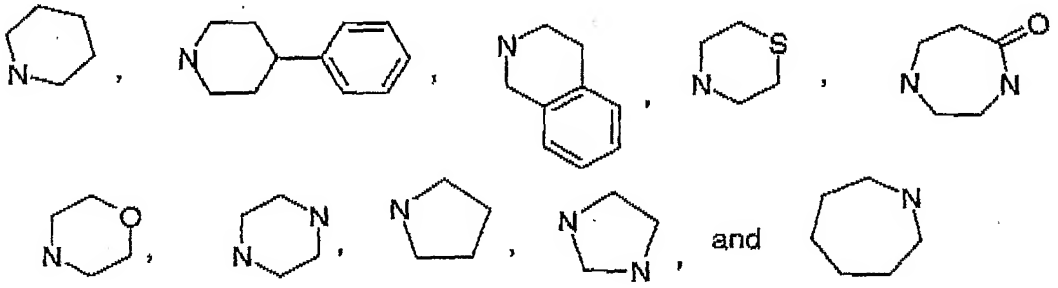
For the groups R^1 and R^2

Preferred R^1 and R^2 groups are independently selected from the group consisting of hydrogen, methyl, ethyl, propyl, pentyl, and isopropyl. Also preferred are R^1 and R^2 groups independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, phenyl,



each of which is optionally substituted with a group selected from the group consisting of halogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 thioalkyl, C_1-C_8 alkylamino, phenyl, C_1-C_8 alkylsubstituted phenyl, C_4-C_8 heterocycle or C_1-C_4 alkyl heterocycle; or combine with a group selected from C_1-C_8 alkyl, halogen, C_1-C_8 haloalkyl, C_1-C_8 thioalkyl, C_1-C_8 alkylamino, phenyl, C_1-C_8 alkylsubstituted phenyl, C_4-C_8 heterocycle or C_1-C_4 alkyl heterocycle to form a substituted or unsubstituted bicycle or tricycle.

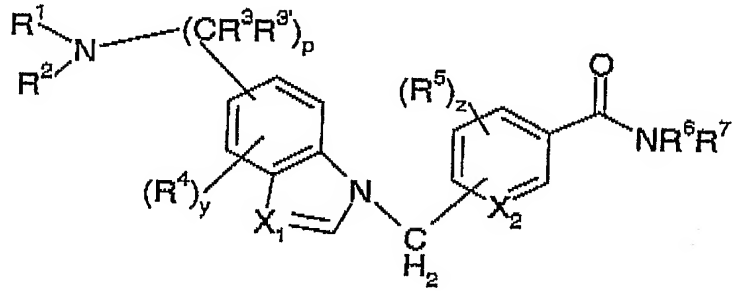
Also preferred are R1 and R2 groups which combine with each other to form a group selected from the group consisting of



Replacement 39

We claim:

1. A compound of formula (I)



(I)

p is 0, 1, or 2;

y is 0, 1, or 2; and z is 0, 1, or 2;

X_1 is CH_2, CH, or N; to form a indolinyl, indolyl, or benzimidazole ring respectively and including applicable double bonds and/or hydrogen atoms;

X_2 is CH or N;

R^1 and R^2 are independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, C_1-C_{10} alkylaryl, SO_2R^8, $(CH_2)_nC(O)NR^8R^8$, SO_2C_1-C_{10} alkylaryl, SO_2C_1-C_8 alkylheterocyclic, C_4-C_{10} alkylcycloalkyl, $(CH_2)_nC(O)OR^8$, and $(CH_2)_nC(O)R^8$; wherein each of the alkyl, alkenyl, and aryl groups are optionally substituted with one to two groups independently selected from C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, C_3-C_8 cycloalkyl, C_1-C_8 alkylaryl, and $C(O)C_1$-C_8 alkyl; and wherein R^1 and R^2 may optionally combine with each other to form a 4, 5, 6, or 7-membered nitrogen-containing heterocycle which nitrogen -containing heterocycle may further have substituents selected from the group consisting of oxo, amino, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, C_1-C_3 alkylaryl, $C(O)C_1$-C_8 alkyl, $CO(O)C_1$-C_8 alkyl, halo, C_1-C_3 haloalkyl; provided that when X is CH, one of R^1 and R^2 is not SO_2H, $CONHSO_2R^8$, CO_2H, or COR^8;

R^3 and $R^{3'}$ are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, aryl, C_1-C_8 alkylcycloalkyl, and C_1-C_8 alkylaryl;

R^4 and R^5 are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkoxy, halo, C_1-C_8 haloalkyl, phenyl, aryl, C_1-C_6 alkylaryl, $(CH_2)_mNSO_2C_1$-C_8 alkyl, $(CH_2)_mNSO_2$phenyl, $(CH_2)_mNSO_2$aryl, $-C(O)C_1$-C_8 alkyl, and

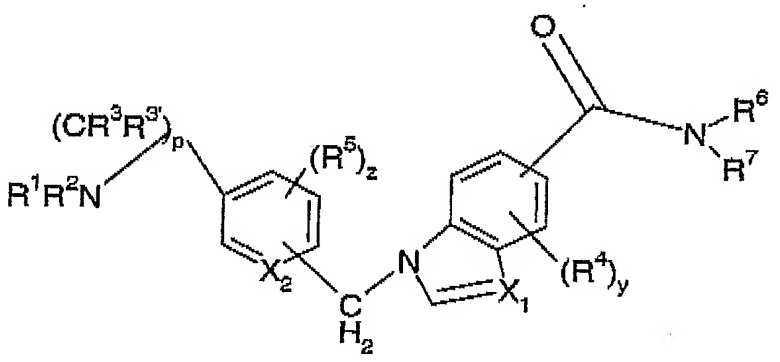
Replacement 40

-C(O)OC$_1$-C$_8$ alkyl; wherein each R^4 and R^5 is attached to its respective ring only at carbon atoms; wherein m is 1 or 2; and n is 1, 2, or 3;

R^6 and R^7 are each independently selected from hydrogen, C$_1$-C$_8$ alkyl, C$_2$-C$_8$ alkenyl, C$_2$-C$_8$ alkynyl, C(O)C$_1$-C$_8$ alkyl, SO$_2$C$_1$-C$_8$ alkyl, SO$_2$C$_1$-C$_8$ alkylaryl, SO$_2$C$_1$-C$_8$ alkylheterocyclic, aryl, C$_1$-C$_8$ alkylaryl, C$_3$-C$_7$ cycloalkyl, C$_1$-C$_6$ alkylcycloalkyl, $(CH_2)_mC(O)OR^8$, $(CH_2)_mC(O)R^8$, $(CH_2)_mC(O)NR^8R^8$, and $(CH_2)_mNSO_2R^8$; wherein each of the alkyl, alkenyl, and aryl groups are optionally substituted with one to two groups independently selected from C$_1$-C$_8$ alkyl, C$_2$-C$_8$ alkenyl, phenyl, and C$_1$-C$_8$ alkylaryl; and wherein R^6 and R^7 may independently combine with each other, and with the nitrogen atom to which they are attached to form a 4, 5, 6, or 7-membered nitrogen containing heterocycle which nitrogen containing heterocycle may optionally have substituents selected from the group consisting of oxo, amino, C$_1$-C$_8$ alkyl, C$_2$-C$_8$ alkenyl, C$_2$-C$_8$ alkynyl, phenyl, and C$_1$-C$_8$ alkylaryl;

R^8 is independently selected from hydrogen, C$_1$-C$_8$ alkyl, C$_2$-C$_8$ alkenyl, phenyl, benzyl, and C$_5$-C$_8$ alkylaryl; or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer, or mixture of diastereomers thereof.

2. A compound of formula II



II

wherein p is 0, 1, or 2;

y is 0, 1, or 2; and z is 0, 1, or 2;

X_1 is CH_2, CH, or N; to form a indolinyl, indolyl, or benzimidazole ring respectively and including applicable double bonds and/or hydrogen atoms;

X_2 is CH or N;

Replacement 41

R^1 and R^2 are independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, C_1-C_{10} alkylaryl, SO_2R^8, $(CH_2)_nC(O)NR^8R^8$, SO_2C_1-C_{10} alkylaryl, SO_2C_1-C_8 alkylheterocyclic, C_4-C_{10} alkylcycloalkyl, $(CH_2)_nC(O)OR^8$, and $(CH_2)_nC(O)R^8$; wherein each of the alkyl, alkenyl, and aryl groups are optionally substituted with one to two groups independently selected from C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, C_3-C_8 cycloalkyl, C_1-C_8 alkylaryl, and $C(O)C_1$-C_8 alkyl; and wherein R^1 and R^2 may optionally combine with each other to form a 4, 5, 6, or 7-membered nitrogen-containing heterocycle which nitrogen -containing heterocycle may further have substituents selected from the group consisting of oxo, amino, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, C_1-C_3 alkylaryl, $C(O)C_1$-C_8 alkyl, $CO(O)C_1$-C_8 alkyl, halo, C_1-C_3 haloalkyl;

R^3 and $R^{3'}$ are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, aryl, C_1-C_8 alkylcycloalkyl, and C_1-C_8 alkylaryl;

R^4 and R^5 are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkoxy, halo, C_1-C_8 haloalkyl, phenyl, aryl, C_1-C_8 alkylaryl, $(CH_2)_mNSO_2C_1$-C_8 alkyl, $(CH_2)_mNSO_2$phenyl, $(CH_2)_mNSO_2$aryl, $-C(O)C_1$-C_8 alkyl, and $-C(O)OC_1$-C_8 alkyl; wherein each R^4 and R^5 is attached to its respective ring only at carbon atoms; wherein m is 1 or 2; and n is 1, 2, or 3;

R^6 and R^7 are each independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, $C(O)C_1$-C_8 alkyl, SO_2C_1-C_8 alkyl, SO_2C_1-C_8 alkylaryl, SO_2C_1-C_8 alkylheterocyclic, C_1-C_8 alkylaryl, C_3-C_7 cycloalkyl, C_1-C_6 alkylcycloalkyl, aryl, $(CH_2)_mC(O)OR^8$, $(CH_2)_mC(O)R^8$, $(CH_2)_mC(O)NR^8R^8$, and $(CH_2)_mNSO_2R^8$; wherein each of the alkyl, alkenyl, and aryl groups are optionally substituted with one to two groups independently selected from C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, and C_1-C_8 alkylaryl; and wherein R^6 and R^7 may independently combine with each other, and with the nitrogen atom to which they are attached to form a 4, 5, 6, or 7-membered nitrogen containing heterocycle which nitrogen containing heterocycle may optionally have substituents selected from the group consisting of oxo, amino, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, phenyl, and C_1-C_8 alkylaryl; provided that when X is N, one of R^6 or R^7 is not CH_2CH_2COOH;

R^8 is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, phenyl, benzyl, and C_5-C_8 alkylaryl; or a pharmaceutically acceptable salt, solvate, enantiomer, racemate, diastereomer, or mixture of diastereomers thereof.

Replacement 42

3. A compound according to Claim 1 wherein X_1 is CH and X_2 is selected CH.

4. A compound according to Claim 1 wherein X_1 is CH and X_2 is selected N.

5. A compound according to Claim 1 wherein X_1 is N, and X_2 is CH.

6. A compound according to Claim 1 wherein X_1 is N, and X_2 is N.

7. A compound according to Claim 1 wherein y is 0 or 1, and R^4 is independently selected from the group consisting of fluoro, chloro, bromo, methoxy, ethoxy, methyl, ethyl, isopropyl, trifluoromethyl, phenyl, benzyl and ethoxy.

8. A compound according to Claim 1 wherein z is 0 or 1, and R^5 is independently selected from the group consisting of fluoro, chloro, bromo, methoxy, ethoxy, methyl, ethyl, isopropyl, trifluoromethyl, phenyl, and benzyl.

9. A compound according to Claim 2 wherein X_1 is CH and X_2 is selected CH.

10. A compound according to Claim 2 wherein X_1 is CH and X_2 is selected N.

11. A compound according to Claim 2 wherein X_1 is N, and X_2 is CH.

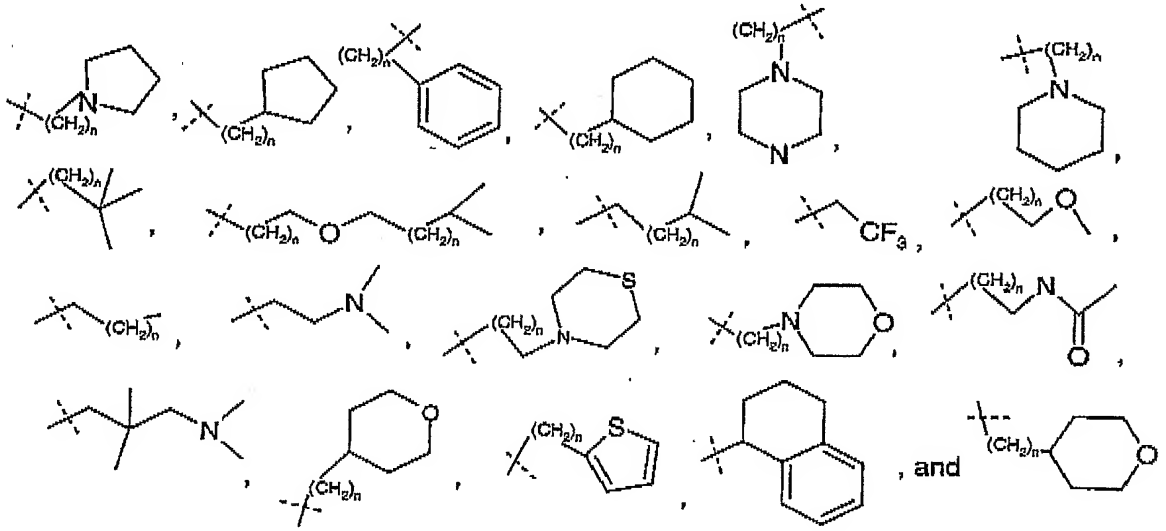
12. A compound according to Claim 2 wherein X_1 is N, and X_2 is N.

13. A compound according to Claim 2 wherein y is 0 or 1, and R^4 is independently selected from the group consisting of fluoro, chloro, bromo, methoxy, ethoxy, methyl, ethyl, isopropyl, trifluoromethyl, phenyl, benzyl and ethoxy.

Replacement 43

14. A compound according to Claim 2 wherein z is 0 or 1, and R^5 is independently selected from the group consisting of fluoro, chloro, bromo, methoxy, ethoxy, methyl, ethyl, isopropyl, trifluoromethyl, phenyl, and benzyl.

15. A compound according to Claim 1 or 2 wherein R^1 and R^2 are each independently selected from the group consisting of hydrogen, methyl, ethyl, propyl, isopropyl, 2-methylpentyl, t-butyl, cyclopropyl, phenyl,



16. The compound according to Claim 1 or 2 wherein R^6 and R^7 are each independently selected from the group consisting of hydrogen, methyl, ethyl, propyl, isopropyl, and phenyl.

17. A compound selected from the group consisting of:
4-{5-[(3-Methyl-butylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-{5-[(2-Thiophen-2-yl-ethylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-{5-[(3,3-Dimethyl-butylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-{5-[(2-Thiophen-2-yl-ethylamino)-methyl]-2,3-dihydro-indol-1-ylmethyl}-benzamide,
4-{5-[(3-Methyl-butylamino)-methyl]-2,3-dihydro-indol-1-ylmethyl}-benzamide,
4-{5-[(3,3-Dimethyl-butylamino)-methyl]-2,3-dihydro-indol-1-ylmethyl}-benzamide,
4-(5-Hexylaminomethyl-indol-1-ylmethyl)-benzamide,

Replacement 44

4-{5-[(3-Phenyl-propylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-(5-{[2-(2-Fluoro-phenyl)-ethylamino]-methyl}-indol-1-ylmethyl)-benzamide,
4-{5-[(2-Hydroxy-ethylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-(5-{[2-(4-Methoxy-phenyl)-ethylamino]-methyl}-indol-1-ylmethyl)-benzamide,
4-{5-[(2-Chloro-6-fluoro-benzylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-{5-[(2-Pyridin-3-yl-ethylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-(5-{[2-(2-Ethoxy-phenyl)-ethylamino]-methyl}-indol-1-ylmethyl)-benzamide,
4-(5-{[2-(Tetrahydro-pyran-4-yl)-ethylamino]-methyl}-indol-1-ylmethyl)-benzamide,
4-{5-[(2-Cyclohex-1-enyl-ethylamino)-methyl]-indol-1-ylmethyl}-benzamide,
4-(5-{[2-(3-Fluoro-phenyl)-ethylamino]-methyl}-indol-1-ylmethyl)-benzamide,
4-{5-[(2-Ethyl-butylamino)-methyl]-indol-1-ylmethyl}-benzamide,
1-{4-[(3-Methyl-butylamino)-methyl]-benzyl}-2,3-dihydro-1H-indole-5-carboxylic acid amide or a pharmaceutically acceptable salt, solvate, enantiomer, diastereomer and diastereomeric mixture thereof.

18. A pharmaceutical composition comprising a compound of Claim 1 or 2 or a pharmaceutically acceptable salt, solvate, enantiomer, diastereomer or diastereomeric mixture thereof in association with a carrier, diluent and/or excipient.

19. A method of treating or preventing obesity and Related Diseases comprising administering a therapeutically effective amount of a compound of Claim 1 or 2.

20. A method according to Claim 19 wherein the Related Diseases is selected from the group consisting of diabetes, diabetic complications, diabetic retinopathy, atherosclerosis, hyperlipidemia, hypertriglycemia, hyperglycemia, and hyperlipoproteinemia.

21. A method of treating and/or preventing diseases related to obesity including irritable bowel syndrome, nausea, vomiting, depression, smoking and alcohol addiction, sexual dysfunction, substance abuse, drug overdose, addictive behavior

disorders, compulsive behaviors, and stroke comprising administering a therapeutically effective amount of a compound of Claim 1 or 2.

22. A method of suppressing appetite in a patient in need thereof, comprising administering a therapeutically effective amount of a compound of Claim 1 or 2.

23. Use of a compound according to Claim 1 or 2 in the manufacture of a medicament for the treatment and/or amelioration of the symptoms associated with obesity and Related Diseases.